REMARKS

Claims 35, 39, 47-54, 56, 57, 59, 60 and 64-79 are now pending. By this Amendment, claims 55, 58 and 61-63 are canceled; claims 39, 47-51, 56, 57, 59, 60 and 66-68 are amended; and claims 69-79 are added.

Applicants appreciate the indication that claims 52-54 and 64 are merely objected to for being dependent upon a rejected base claim. Because it is respectfully submitted that the rejected base claims are allowable, it is respectfully submitted that claims 52-54 and 64 should also be allowed.

Applicants also appreciate the indication that claims 39, 51-59, 61-64, 66 and 68 are deemed free of the prior art. For the reasons discussed herein, it is respectfully submitted that all of the claims are free of the prior art.

Applicants thank Examiner Kallis for the courtesies extended during the August 29, 2005, personal interview. At the interview, the Examiner "agreed to drop the NEW MATTER rejection in view of the support on page 4 of the specification." Applicants' further separate record of the substance of the interview is incorporated into the following remarks.

Claims 61-63 are rejected under 35 U.S.C. §112, first paragraph, for allegedly containing new matter. Applicants respectfully traverse the rejection.

The specification clearly recites that "the present invention relates to a polynucleotide substantially comprising a nucleotide sequence which has 50% or more homology to the nucleotide sequence comprised in SEQ-ID-No.:1." The specification also indicates that the phrase "the nucleotide sequence comprised in SEQ-ID-No.: 1" means "the nucleotide sequence of SEQ-ID-No.: 1 or a part of the nucleotide sequence." Page 4, lines 4-9 (emphasis added). Furthermore, the specification recites that the "above-mentioned homology is preferably 70% or more, more preferably 80% or more, still more preferably 90 % or more, and especially 95% or

more." Page 4, lines 17-18. Based on these teachings, it was agreed in the interview that the specification clearly supports claims 61-63.

Claims 61-63 are supported by the present specification. Therefore, the new matter rejection of claims 61-63 should be reconsidered and withdrawn.

Claims 35, 39, 47-51, 55-63 and 65-68 are rejected under 35 U.S.C. §112, first paragraph, as allegedly not being supported by the written description. Applicants respectfully traverse the rejection.

Claims 47, 50 and 60 are each independent claims. Claim 50 is directed to an isolated polynucleotide having a sequence of SEQ ID NO:1, and/or the nucleotide sequence fully complementary thereto. As indicated at page 4, lines 1-3, of the Office Action, the subject matter of this claim is clearly supported by the specification.

In addition, it is respectfully submitted that the subject matter of claims 47 and 60 is fully supported by the present specification. As suggested by the Examiner in the interview, claims 47 and 60 have been amended to incorporate the features of claims 58 and 63, respectively. The specification clearly describes polynucleotides encoding for variants of SEQ ID NO: 2, specifically variants in which 1-20 amino acids having been substituted, as recited in claim 47. In addition, the specification clearly describes polynucleotides comprising a nucleic acid sequence encoding 2-hydroxyisoflavanone synthase having at least 95% homology to nucleotides 144-1712 of SEQ ID NO: 1, as recited in claim 60. Furthermore, the specification discloses nucleotide sequence SEQ ID NO: 1, which codes for SEQ ID NO: 2.

The Office Action correctly points out that *University of California v. Eli Lilly & Co.* states that a "description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." However, this statement must be

considered in the context of the facts presented in *Eli Lilly*. In this case, the patentee was claiming vertebrate and mammalian insulin cDNA based on a specification that only described the cDNA sequence encoding insulin in rats. The specification provided no structural information about cDNA encoding insulin in vertebrates or mammals other than rats. In this context, the Federal Circuit held that "a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA,' without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function." *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

In contrast, claim 47 has been amended to recite that, in the variant, 1 to 20 amino acids have been substituted. SEQ ID NO: 2 contains 523 amino acids. Thus, in claim 47, only a small percentage of the amino acids are undefined. As a result, claim 47 clearly provides "a recitation of structural features common to the members of the genus," these features constituting a substantial portion of the genus. In addition, this structural description of the variants is clearly "sufficient to distinguish [the claimed subject matter] from other materials," as required by *Eli Lilly*. 43 USPQ2d at 1405.

In addition, claim 60 recites a polynucleotide comprising a nucleic acid sequence encoding 2-hydroxyisoflavanone synthase having at least 95% homology to nucleotides 144-1712 of SEQ ID NO: 1 and/or a full complement of this nucleic acid sequence. Thus, as with claim 47, claim 60 clearly provides "a recitation of structural features common to the members of the genus," these features constituting a substantial portion of the genus. Specifically, claim 60 indicates that all members of the genus have at least 95% homology to nucleotides 144-1712 of SEQ ID NO: 1 and/or its full complement. In addition, this structural description, is clearly "sufficient to distinguish [the claimed subject matter] from other materials."

As pointed out in the Office Action, in addition to these structural limitations, claims 47 and 60 contain functional limitations. Specifically, claim 47 recites that the variant catalyzes the synthesis of 2-hydroxyisoflavanone from flavanone in leguminous plants. In addition, claim 60 recites that the nucleic acid sequence encodes 2-hydroxyisoflavanone synthase. However, the Federal Circuit has not held that a claim reciting a functional limitation, together with a recitation of substantial structural features common to the members of the genus, does not have written description in a specification. Instead, *Eli Lilly* merely held that identifying a cDNA by its function alone is insufficient.

The specification clearly supports the current claims. Therefore, the written description rejection should be reconsidered and withdrawn.

Claims 35, 39, 47-51, 55-63 and 65-68 are rejected under 35 U.S.C. §112, first paragraph, for allegedly lacking enablement in the specification. Applicants respectfully traverse the rejection.

To fulfill the enablement requirement, the specification must describe how to make and use the full scope of the invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). However, the scope of enablement must only bear a "reasonable correlation" to the scope of the claims. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

The Office Action argues that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims. In particular, the Office Action indicates that the specification fails to teach which amino acids of SEQ ID NO:2 can be deleted, substituted or added and still produce a protein with the same function as the protein of SEQ ID NO:2.

It is noted initially that this argument does not appear to apply to independent claim 50, which recites an isolated polynucleotide having the sequence of SEQ ID NO:1 and/or the nucleotide sequence fully complementary thereto.

In addition, with regard to independent claims 47 and 60, as suggested by the Examiner during the interview, these claims have been amended to incorporate the features of claims 58 and 63, respectively. It is respectfully submitted that one of ordinary skill in the art would have been able to make and use polynucleotides within claims 47 and 60 without undue experimentation. In particular, although a single amino acid change can affect the ability of a protein to function, one of ordinary skill in the art is well aware of the types of changes that are less likely to affect the ability of a protein to function. In addition, modifying and testing the function of a protein would have been considered routine experimentation in the art. In addition, the specification, at pages 25-29, specifically describes a test for determining whether a protein is a 2-hydroxyisoflavanone synthase, which catalyzes the synthesis of 2-hydroxyisoflavanone from flavanone.

Furthermore, the specification provides guidance as to amino acid substitutions that can be made. In particular, the specification indicates that

> an amino acid residue can be replaced by a different amino acid residue with similar characteristics. The typical substitution may be a substitution between Ala, Val, Leu, and Ile, between Ser and Thr, between the acid residue Asp and Glu, between Asn and Gln, between the basic residues Lys and Arg, or between the aromatic residues Phe andTyr.

Page 3, lines 6-11. This in turn provides guidance as to changes that can be made to the claimed polynucleotides while retaining the claimed functional properties.

Given the guidance provided in the specification, together with the knowledge of one of ordinary skill in the art, it is respectfully submitted that the present claims are enabled by the specification. Thus, the enablement rejection should be reconsidered and withdrawn.

Claims 35, 47-50, 60, 65 and 67 are rejected under 35 U.S.C. §102 over Siminszky et al. Applicants respectfully traverse the rejection.

Independent claims 47, 50 and 60 have been amended substantially as suggested by the Examiner. Thus, the teaching of a sequence that is complementary to SEQ ID NO: 1 over nucleotides 439-466 of SEQ ID NO: 1 does not anticipate the present claims. Therefore, the rejection over Siminszky should be reconsidered and withdrawn.

Claims 69-79 have been added herein to further define the invention. Claims 69 and 70 are each independent claims similar to previous claims 55 and 60, respectively, except that each claim recites that the nucleic acid sequence is a naturally-occurring sequence. Claim 73 is an independent claim similar to previous claim 47, which recites that the variant is a natural variant. Claims 71 and 72 depend from claim 70. Claims 74-79 depend from claim 73.

In the present application, the polynucleotide sequence coding for 2-hydroxyisoflavanone synthase (hereinafter "IFS") of licorice has been revealed. This sequence, SEQ ID NO: 1, belongs to the subfamily CYP93C.

When a new amino acid sequence of cytochrome P450 is registered in a database, it is classified based on the homology of its amino acid sequence to a known sequence. If the amino acid sequence has 55% or more homology to a known sequence, it is classified as being in the same subfamily as the known sequence. Thus, when a new amino acid sequence having 55% or more homology to this sequence is found, it is classified as belonging to the subfamily CYP93C. It is well known that cytochrome P450s belonging to the same subfamily have the same or substantially similar function at quite high probability. Accordingly, since claims 69-79 have been restricted to naturally-occurring sequences, almost all such amino acid sequences having 55% or more homology to SEQ ID NO: 2 would function as IFS. In addition, almost all naturally-occurring nucleotide sequences having 70% or more homology to SEQ ID NO: 1 would code for IFS. Contrary to the statement made in the Office Action that only one amino

acid substitution could result is a polypeptide that does not encode IFS, although it may be possible to prepare an artificial sequence in which this is the case, with regard to naturally-occurring sequences, this would not be the case.

In fact, the sequences originating from soybean, Lotus Japonicus, Trifolium pretense, and Medicago truncaturla have been actually registered as CYP93C. In addition, they have been proved to function as IFS. Furthermore, they have 80% or more homology to SEQ ID NO: 2. In addition, there has not been reported a polynucleotide originating from leguminous plants that has 70% or more homology to SEQ ID NO: 2 that does not function as IFS.

In addition, based on this teaching of SEQ ID NO: 1, it has been made possible to find, with only routine experimentation, naturally-occurring sequences coding for IFS originating from other plants, particularly from leguminous plants, using SEQ ID NO: 1 in a homology search or the like. Such a method of obtaining the sequence by an homology search is well known in the art. In addition, a method for confirming IFS function is well known in the art and also described in the present application.

For all of these reasons, it is respectfully submitted that claims 69-79 have written description and are enabled by the present specification. In addition, these claims are not anticipated by Siminszky for the same reason as the claims discussed above.

In view of the foregoing, it is respectfully submitted that this application is in condition for allowance. Favorable reconsideration and prompt allowance of claims 35, 39, 47-54, 56, 57, 59, 60 and 64-79 are earnestly solicited.

Should the Examiner believe that anything further would be desirable in order to place this application in even better condition for allowance, the Examiner is invited to contact the undersigned at the telephone number set forth below.

Respectfully submitted,

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